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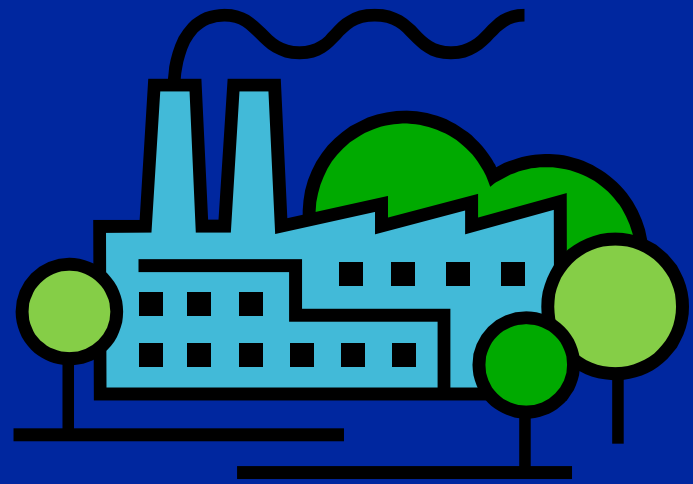
Post-marketing Activities

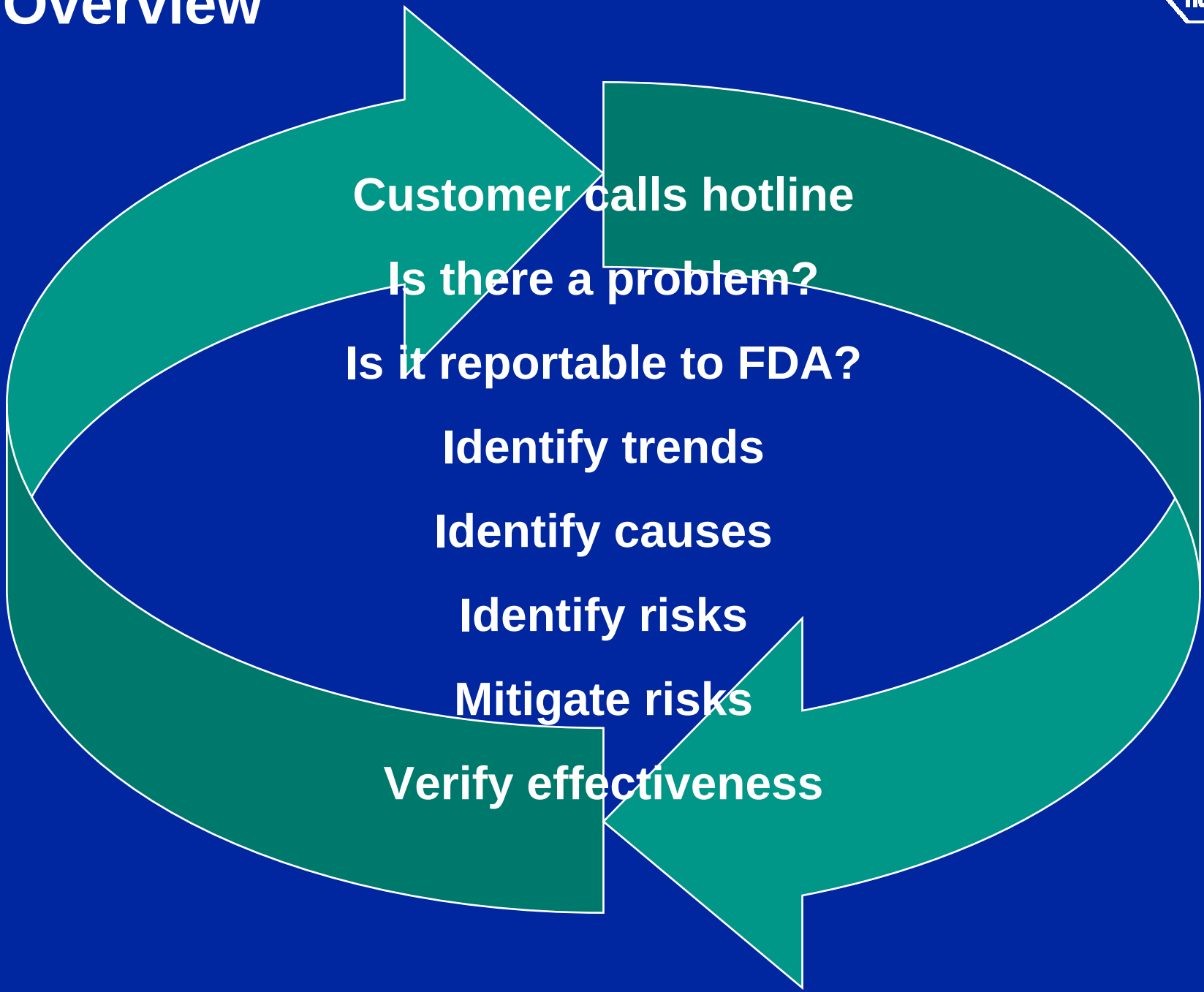
Industry Perspective

Luann Ochs, MS

CLIAC, Feb 11, 2004



Overview



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The Regulations

Quality System Regulation, 21 CFR Part 820

- 820.198 Complaint Files

Each manufacturer shall establish procedures for receiving, reviewing, and evaluating complaints

-- Timely processing

-- Documented

-- Determine whether the complaint represents an event that is required to be reported to FDA

The Regulations, continued

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Quality System Regulation, 21 CFR Part 820

- 820.100 Corrective and Preventive Action (CAPA)

  Each manufacturer shall establish and maintain procedures for implementing corrective and preventive action
  -- Analyze processes, quality audit reports, quality records,
  service records, complaints, returned product
  -- Identify existing and potential causes of nonconforming
  product or quality problems
  -- Identify actions needed to correct and prevent
  recurrence
  -- Verify or validate corrective or preventive action

The Regulations, continued

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Medical Device Reporting (MDR), 21 CFR 803

Device user facilities, importers, and manufacturers must report to FDA when a device has, or may have caused or contributed to a death or serious injury

-- Adverse event files

-- Submit summary reports to FDA

-- Time requirements: 30 days, or 5 days if remedial action is needed to prevent further risk of harm to public health

Customer Calls Aid Continuous Improvement

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Companies utilize customer calls for

- Fulfilling Regulatory obligations, as well as for
- Continuous product improvement
- Promote customer satisfaction

Customer Calls the Hotline

Allegation of death or serious injury?

YES

- Get all details of incident
- Follow procedures for MDR reporting to FDA
- Analyze retentions or returns, looking for product quality issues
- CAPA?

NO

- Phone solve
- Troubleshoot
  -- May send product
- Replace
  -- May request product return for analysis
- Trend analysis
- CAPA?

Risk

Trend Analysis

- Vast majority of CAPAs are result of trend analysis
- Complaint data compiled over time
- Break down data, e.g.:
  -- by product
  -- by specific complaint
  -- by resolution of complaint
  -- by identified failure

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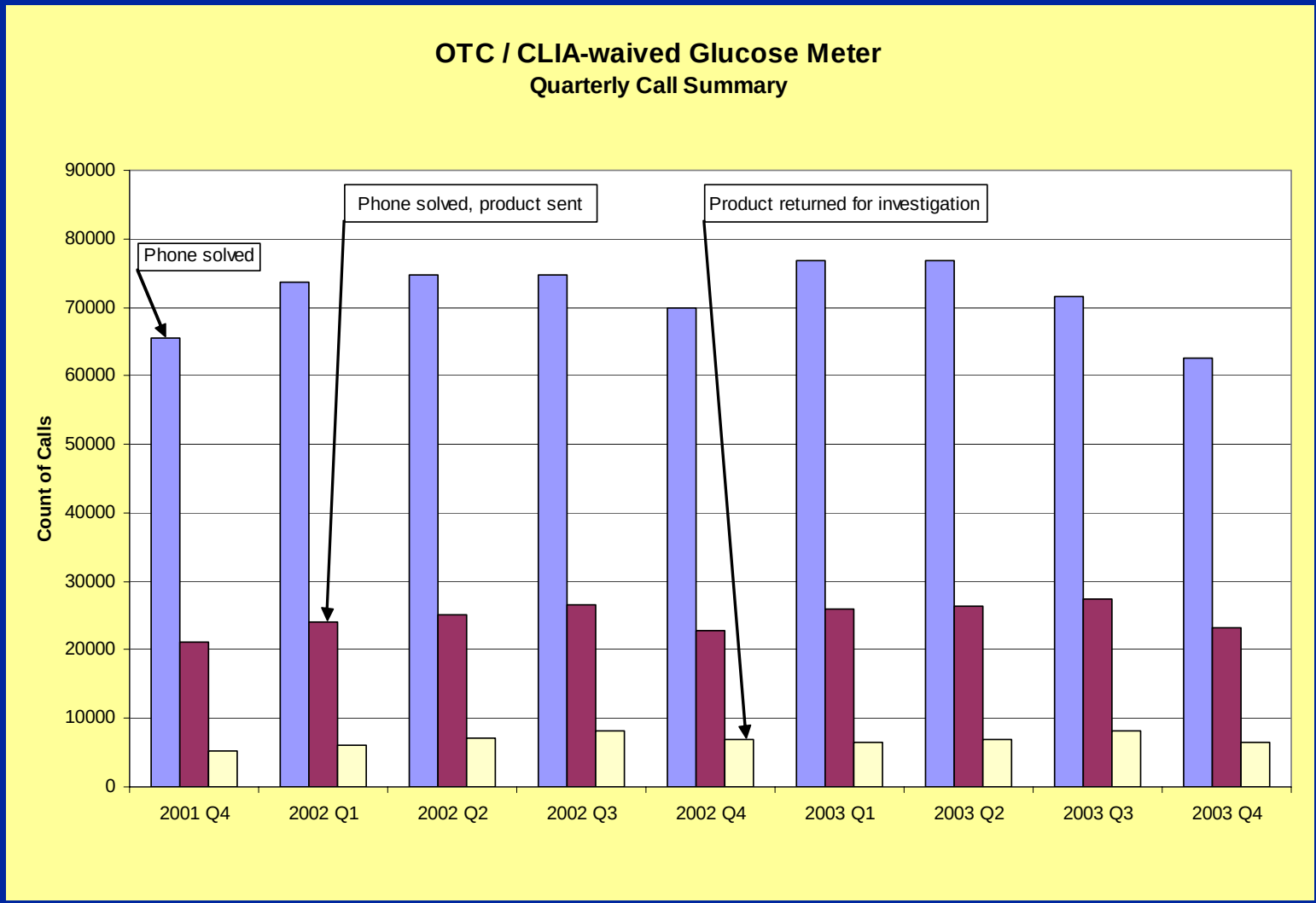
Total Calls & Resolution



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Returned Product Analysis

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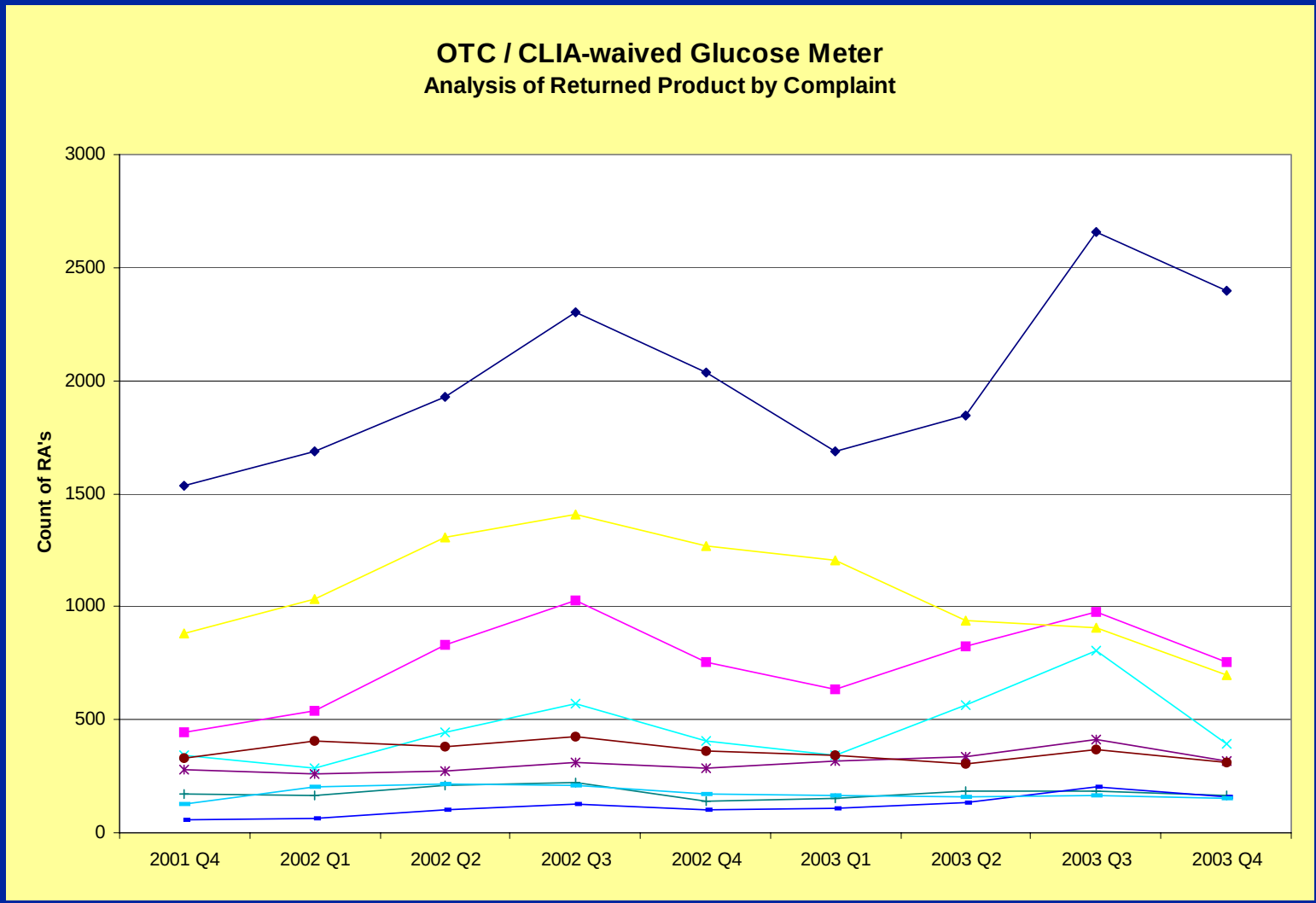
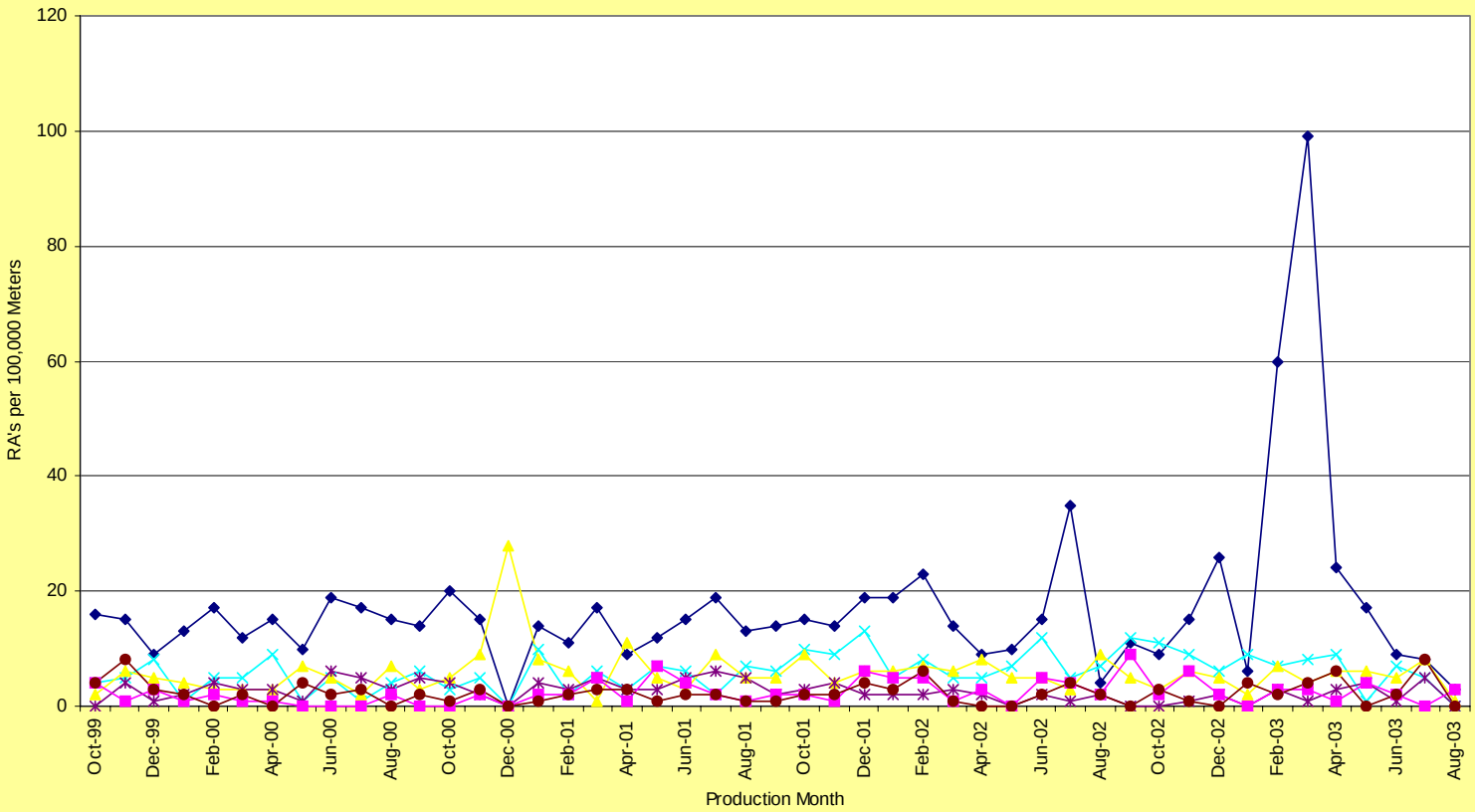


Return Analysis, Normalized



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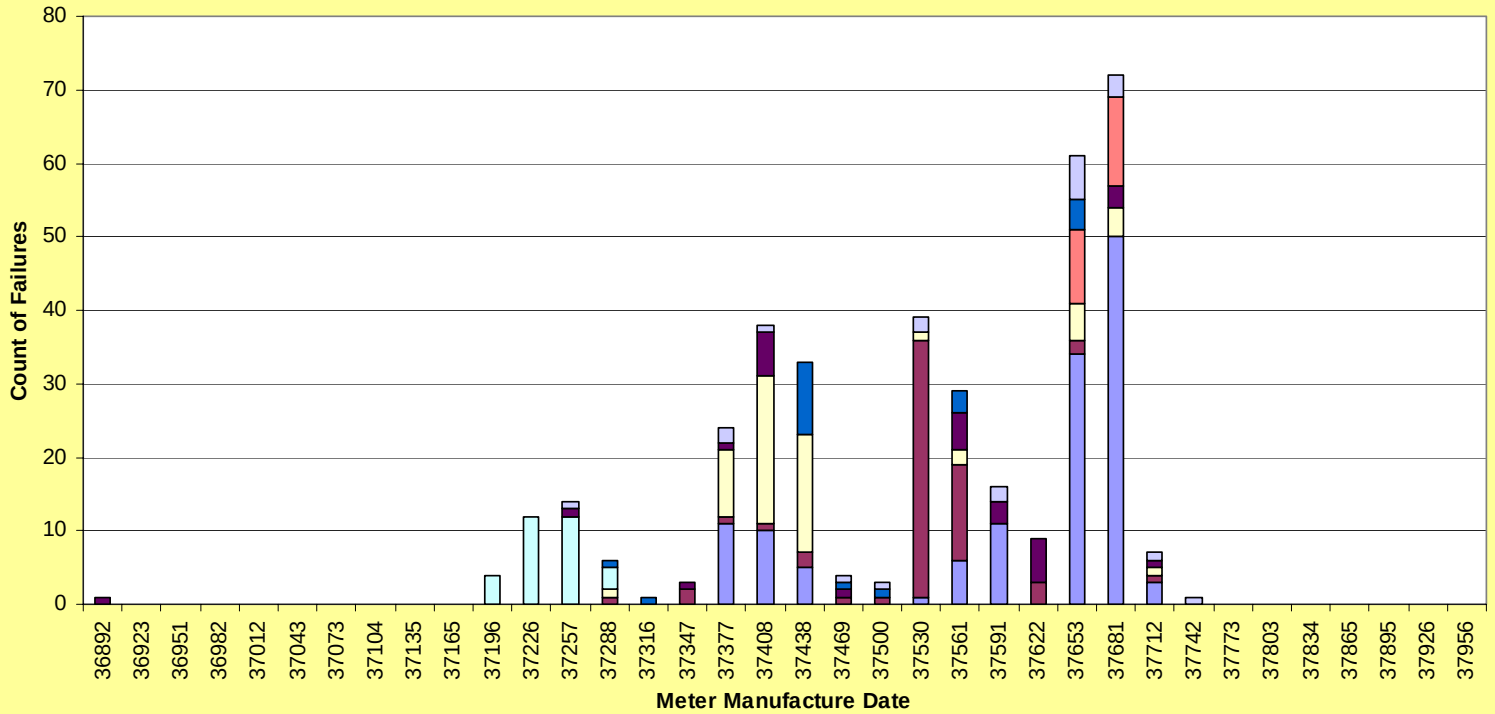
Failure Analysis



Risk Management Principles

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1. ***Identify the hazards***

   -- **FMEA, FTA**
   Example FMEA template

   -- NCCLS EP 18
   EP-18 Examples

Source: FDA Guidance "Device Use Safety, Incorporating Human Factors in Risk Management, Aug 1999.

Example FMEA template

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Possible Hazard	Effect	Potential Causes	Minimum Requirement for safety	Controls	S	O	D	RPN

Risk Management Principles

1. ***Identify the hazards***

   -- FMEA, FTA
   Example FMEA template

   -- NCCLS EP 18
   EP-18 Examples

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EP-18 Example 1

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Appendix A. Example of a "System-Specific Sources of Error" Matrix

Potential Sources of Error	Applicable Y/N?	Nature of Impact	Training/Laboratory Procedure Requirements	Applicable Quality Monitoring	Frequency of Monitoring
1 Specimen Collection					
1.1 Contamination					
1.1.1 Alcohol					
1.1.2 Other Cleansing Agent					
1.1.3 Anticoagulants in Lines					
1.1.4 Intravenous Fluids					
1.1.5 Admixture with Other Fluids/Materials					
1.2 Inadequate Sample					
1.2.1 Poor Circulation at Sample Site					
1.2.2 Poor Vascular Access					
1.2.3 Not Enough Collected					
1.2.4 Poor Technique					
1.2.5 Too Much Collected					
1.3 Hemolysis					
1.4 Incorrect Patient Drawn					
1.5 Inappropriate Sample					
1.5.1 Arterial vs. Venous vs. Capillary					
1.5.2 Whole Blood vs. Plasma					
1.5.3 Sample in Wrong Container or Syringe/Wrong Additives					
1.5.4 Fasting vs. Nonfasting					
1.5.5 Clotted Sample					
1.5.6 Inappropriate Time of Collection					
1.6 Patient Condition Inappropriate for Testing Method					

EP-18 Example 2

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Appendix A. (Continued)

Potential Sources of Error	Applicable Y/N?	Nature of Impact	Training/Laboratory Procedure Requirements	Applicable Quality Monitoring	Frequency of Monitoring
4.5 Calculation Required					
5 Preliminary Review					
5.1 Improper Interpretation of Control Results					
5.2 Outlier/Nonsense Result Not Recognized					
5.3 Result Outside of Linear Range Not Recognized					
5.4 Alert Value Not Recognized					
5.5 Need for a Confirmatory Sample Not Recognized					
5.6 Effect of Preanalytical Variables Not Recognized					
5.7 Instrument Malfunction Not Recognized					
5.8 Interference Not Recognized					
6 Integration/Report into Chart					
6.1 No Result Recorded					
6.2 Result Recorded in Incorrect Patient Chart					
6.3 Incorrect Information Recorded					
6.3.1 Data					
6.3.2 Time					
6.3.3 Result					
6.4 Information Unreadable					

Risk Management Principles, continued

2. ***Develop strategies and controls to eliminate, reduce likelihood of, or mitigate the consequences***

- Remove hazard causes through design
- Make design error tolerant
- Alert users
- Develop written procedures and training for safe operation (labeling and training materials)

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Risk Management Principles, continued

3. Verify that controls are effective, e.g.:

- Validation
- Stress testing
- Human factors testing
- User studies

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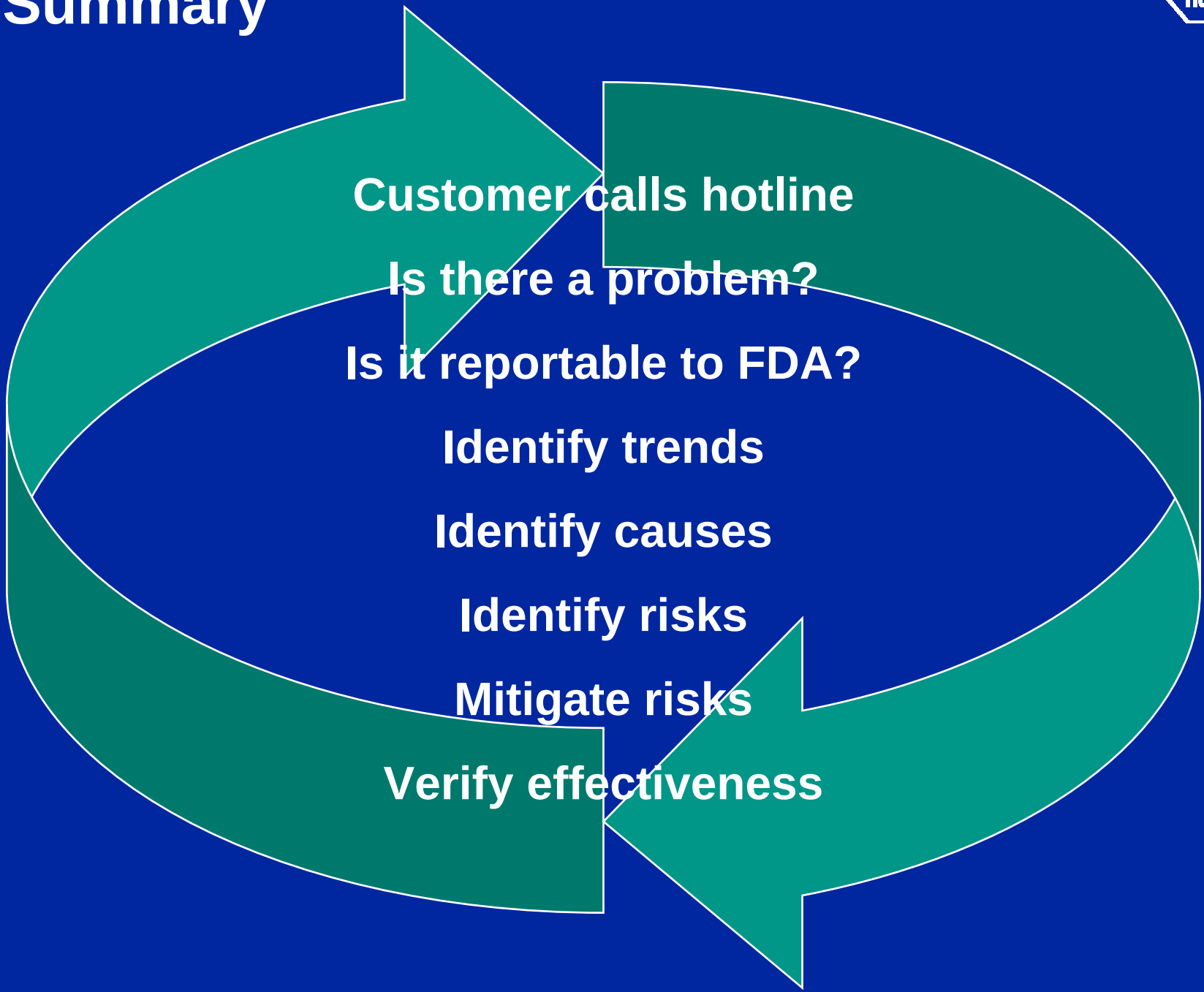
Summary



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